

**AMENDMENT UNDER 37 C.F.R. § 1.111**  
**U.S. Appl. No. 09/368,670**

wherein  $R_{11a}$  is H;  $C_{1-10}$  alkyl;  $C_6$  aryl;  $C_{7-10}$  alkylaryl;  $C_{3-7}$  cycloalkyl or  $C_{4-8}$  (alkylcycloalkyl) optionally substituted with carboxyl; or heterocycle- $C_{1-6}$  alkyl;

and  $R_{11b}$  is  $C_{1-6}$  alkyl substituted with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl or phenylmethoxycarbonyl; or  $C_{7-16}$  aralkyl substituted on the aromatic portion with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl or phenylmethoxycarbonyl;

or  $R_{11a}$  and  $R_{11b}$  are joined to form a 3 to 7-membered nitrogen-containing ring optionally substituted with carboxyl or ( $C_{1-6}$  alkoxy) carbonyl;

or

b) when Q is N-Y, a is 0 or 1, b is 0 or 1, and

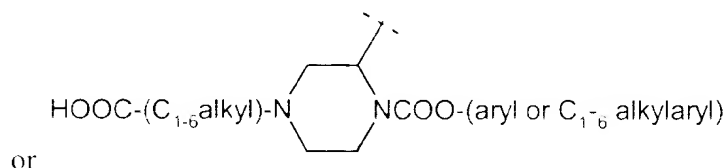
B is H, an acyl derivative of formula  $R_{11}-C(O)-$  or a sulfonyl of formula  $R_{11}-SO_2$  wherein

$R_{11}$  is (i)  $C_{1-10}$  alkyl optionally substituted with carboxyl or  $C_{1-6}$  alkanoyloxy;  $C_{1-6}$  alkoxy; or carboxyl substituted with 1 to 3  $C_{1-6}$  alkyl substituents;

(ii)  $C_{3-7}$  cycloalkyl or  $C_{4-10}$  alkylcycloalkyl, both optionally substituted with carboxyl, ( $C_{1-6}$  alkoxy)carbonyl or phenylmethoxycarbonyl;

(iii)  $C_6$  or  $C_{10}$  aryl or  $C_{7-16}$  aralkyl optionally substituted with  $C_{1-6}$  alkyl, hydroxy, or amino optionally substituted with  $C_{1-6}$  alkyl; or

(iv) Het optionally substituted with  $C_{1-6}$  alkyl, hydroxy, amino optionally substituted with  $C_{1-6}$  alkyl, or amido optionally substituted with  $C_{1-6}$  alkyl,



$R_6$ , when present, is  $C_{1-6}$  alkyl substituted with carboxyl;

$R_5$ , when present, is  $C_{1-6}$  alkyl optionally substituted with carboxyl;

and

c) when Q is either  $CH_2$  or N-Y, then

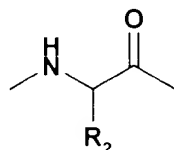
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R<sub>4</sub> is C<sub>1-10</sub> alkyl, C<sub>3-7</sub> cycloalkyl or C<sub>4-10</sub> (alkylcycloalkyl);

z is oxo or thioxo;

R<sub>3</sub> is C<sub>1-10</sub> alkyl optionally substituted with carboxyl, C<sub>3-7</sub> cycloalkyl or C<sub>4-10</sub> (alkylcycloalkyl);

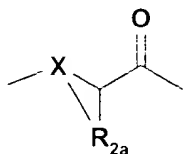
W is a group of formula II:



Formula II

wherein R<sub>2</sub> is C<sub>1-10</sub> alkyl or C<sub>3-10</sub> cycloalkyl optionally substituted with carboxyl or an ester or amide thereof; C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl; or

W is a group of formula IIa:



Formula IIa

wherein X is CH or N; and

R<sub>2a</sub> is divalent C<sub>3-4</sub> alkylene which together with X and the carbon atom to which X and R<sub>2a</sub> are attached form a 5- or 6-membered ring, said ring optionally substituted with OH; SH; NH<sub>2</sub>; carboxyl; R<sub>12</sub>; CH<sub>2</sub>-R<sub>12</sub>, OR<sub>12</sub>, C(O)OR<sub>12</sub>, SR<sub>12</sub>, NHR<sub>12</sub> or NR<sub>12</sub>R<sub>12a</sub>[:];

wherein R<sub>12</sub> and R<sub>12a</sub> are independently a saturated or unsaturated C<sub>3-7</sub> cycloalkyl or C<sub>4-10</sub> (alkyl cycloalkyl) being optionally mono-, di- or tri-substituted with R<sub>15</sub>,

or R<sub>12</sub> and R<sub>12a</sub> is a C<sub>6</sub> or C<sub>10</sub> aryl or C<sub>7-16</sub> aralkyl optionally mono-, di- or tri-substituted with R<sub>15</sub>, or R<sub>12</sub> and R<sub>12a</sub> is Het or (lower alkyl)-Het optionally mono-, di- or tri-substituted with R<sub>15</sub>.

wherein each R<sub>15</sub> is independently C<sub>1-6</sub> alkyl; C<sub>1-6</sub> alkoxy; amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; sulfonyl; NO<sub>2</sub>; OH; SH; halo; haloalkyl; amido optionally mono-substituted with C<sub>1-6</sub> alkyl, C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-16</sub> aralkyl, Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C<sub>6</sub> or C<sub>10</sub> aryl, C<sub>7-16</sub> aralkyl or

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Het, said aryl, aralkyl or Het being optionally substituted with R<sub>16</sub>;

wherein R<sub>16</sub> is C<sub>1-6</sub> alkyl; C<sub>1-6</sub> alkoxy; amino optionally mono- or di-substituted with C<sub>1-6</sub> alkyl; sulfonyl; NO<sub>2</sub>; OH; SH; halo; haloalkyl; carboxyl; amide; or (lower alkyl)amide;

or X is CH or N; and R<sub>2a</sub> is a divalent C<sub>3-4</sub> alkylene which together with X and the carbon atom to which X and R<sub>2a</sub> are attached form a 5- or 6-membered ring which in turn is fused with a second 5-, 6- or 7-membered ring to form a bicyclic system wherein the second ring is substituted with OR<sub>12a</sub> wherein R<sub>12a</sub> is C<sub>7-16</sub> aralkyl;

R<sub>1a</sub> is hydrogen, and R<sub>1</sub> is the side chain of an amino acid selected from the group consisting of cysteine (Cys), aminobutyric acid (Abu), norvaline (Nva) and allylglycine (AlGly); or

R<sub>1a</sub> and R<sub>1</sub> together form a 3- to 6-membered ring optionally substituted with R<sub>14</sub> wherein R<sub>14</sub> is C<sub>1-6</sub> alkyl, C<sub>3-5</sub> cycloalkyl, C<sub>2-6</sub> alkenyl, C<sub>2-6</sub> alkynyl, C<sub>6</sub> aryl or C<sub>7-10</sub> aralkyl all optionally substituted with halo; and

A is hydroxy [or a pharmaceutically acceptable salt of ester thereof]; or C<sub>1-6</sub> alkylamino, di(C<sub>1-6</sub> alkyl)amino or phenyl-C<sub>1-6</sub> alkylamino;

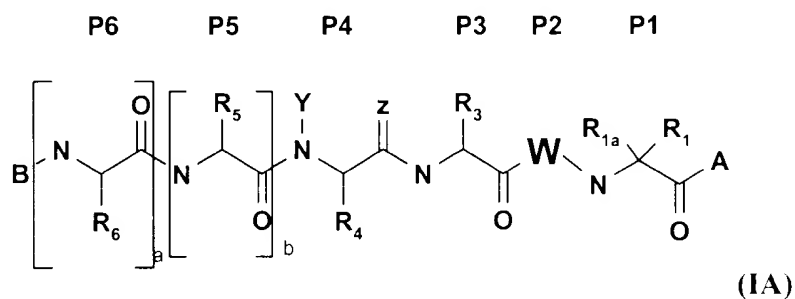
or a pharmaceutically acceptable salt or ester thereof.

Claim 23, line 7 (page 153, line 4), after "position with" insert --R<sub>13</sub>, wherein --;  
line 8 (page 153, line 5), after "or 2, and" delete -- R<sub>13</sub>, wherein --.

Claim 32, line 3, delete "all of which" and insert --each of which is--.

40. (Amended) A compound of formula (IA) [including] or the racemates, diastereoisomers [and] or optical isomers thereof

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wherein Y is H or C<sub>1-6</sub> alkyl;

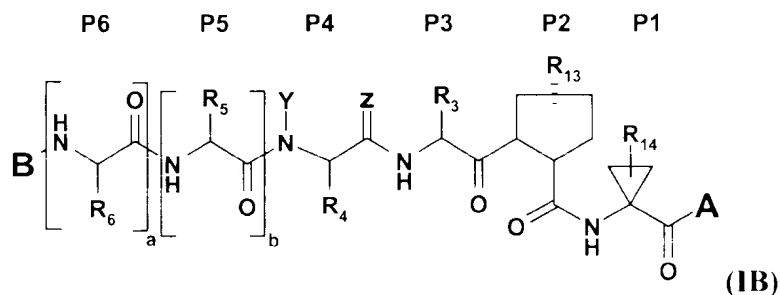
a is 0 or 1;

b is 0 or 1;

B is as defined in claim 1, paragraph b);

R<sub>6</sub>, R<sub>5</sub>, R<sub>4</sub>, Z, R<sub>3</sub>, W, R<sub>1</sub>, R<sub>1a</sub> and A are as defined in claim 1.

45. (Amended) A compound of formula IB [including] or the racemates, diastereoisomers [and] or optical isomers thereof:



wherein

B, a, b, R<sub>6</sub>, R<sub>5</sub>, Y, R<sub>4</sub>, Z, R<sub>3</sub>, and A are as defined in claim 1,

R<sub>13</sub> is R<sub>12</sub>, OR<sub>12</sub>, C(O)OR<sub>12</sub>, SR<sub>12</sub>, NHR<sub>12</sub> or NR<sub>12</sub>, wherein R<sub>12</sub> and R<sub>12a</sub> are as defined in claim 1; and

R<sub>14</sub> is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl optionally substituted with halogen; C<sub>6-10</sub> aryl or C<sub>7-10</sub> aralkyl optionally substituted with halogen; or a pharmaceutically acceptable salt or ester

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thereof.

6.3  
Claim 54, line 2, delete "naphthylmethoxy" and insert --naphthylmethoxy--.

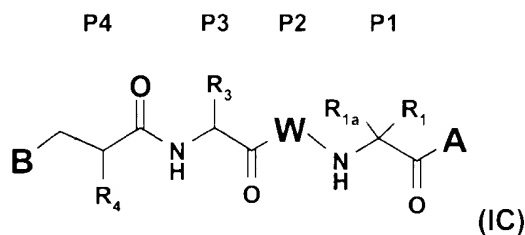
6.4  
Claim 58, line 1, delete "the P1 segment" and insert --P1--.

Claims 59 and 60, line 1 of each claim, delete "said P1 segment" and insert --P1--.

Claim 61, delete "said asymmetric carbon at position 1" and insert --the C<sub>1</sub> carbon atom--.

Claim 63, line 2, delete "all of which" and insert --each of which is--.

67. (Amended) A compound of formula IC [including] or the racemates,  
diastereoisomers [and] or optical isomers thereof:



5  
wherein B is as defined in claim 1, paragraph a);

R<sub>4</sub>, R<sub>3</sub>, W, R<sub>1a</sub>, P<sub>2</sub>, and A are as defined in claim 1.

Claim 96, line 2, delete "therapeutically" and insert --pharmaceutically--.